### REMARKS/ARGUMENTS

### I. SUPPORT FOR THE CLAIM AMENDMENTS

In response to the Final Office Action, dated July 29, 2005, the Advisory Action, dated October 4, 2005, Applicants submitted proposed claim amendments on October 31, 2005 in accordance with the guidance the Examiner provided in the Interview of September 1, 2005. The amendments to the claims, however, were not entered. Submitted herewith is a claim set that incorporates the Examiner's comments and suggestion in the Interview of September 1, 2005, as well as the comments contained in the Advisory Action of October 4, 2005. Accordingly, claims 1, 6 and 12 have been amended, and claims 10 and 11 have been canceled. Support for the amended claims can be found throughout the specification and the originally presented claims. Specifically, support for the amendments to claims 1 and 6 can be found at least in paragraphs 0017, 0018, 0026, 0029, 0033 and 0073. Claim 12 was amended to change dependency. Accordingly, the amendments to the claims do not introduce new matter to the present application. Upon entry of the amendments, claims 1-9 and 12-18 would be under consideration.

Also in response to the Examiner's comments in paragraph 11 of the Advisory Action, Applicants assert and restate that the cited art does not anticipate or render obvious the claimed invention. As was established during the personal interview of September 1, 2005, and as has been asserted throughout prosecution, the cited references do not teach or suggest a glucose-galactose periplasmic biding protein (GGBP) with a *weaker* affinity for the target analyte than that of the wild-type GGBP, as the current claims require. Accordingly, the current claims are novel and not obvious over the cited references.

or bringing this perceived grammar error to their attention. Applicants have amended claim 1 accordingly. Withdrawal of this rejection is solicited.

### 3. "And"

In the Office Action, the Examiner alleged that claim 6 was indefinite under 35 U.S.C. §112, second paragraph, "because it is not clear what values are required for calculating a ratio." Office Action, page 5. Without agreeing with the Examiner's assertions, Applicants have amended claim 6 to better capture envisioned commercial embodiments. The amendments to claim 6 render the Examiner's rejection of this claim moot. Reconsideration and withdrawal of this rejection are earnestly solicited.

### 4. "Alexa"

In the Office Action, the Examiner alleged that claim 18 was indefinite under 35 U.S.C. §112, second paragraph, because "the recitation of proprietary trademarks (e.g., "Alexa") is indefinite." Office Action, page 5. Applicants' representative has conducted another search of the USPTO web-accessible trademark database and found no registered trademark of "Alexa" that is associated with a small molecule dye. Previously submitted with the Response to Final Office Action, filed September 2, 2005 was an article (Panchuk-Voloshina, N. et al., J. Histochem. Cytochem. 47(9): 1179-1189 (1999)) that demonstrates that one of skill in the art would understand the term "Alexa dye" has a specific meaning, and that the specific Alexa dyes, e.g., Alexa 532, have a definite structure that is readily understood by one of skill in the art. Reconsideration and withdrawal of this rejection are earnestly solicited.

# B. THE REJECTION OF CLAIMS 1-13 AND 17-18 UNDER 35 U.S.C. §102(b) IS NOW MOOT

In the Office Action, the Examiner rejected claims 1-13 and 17-18 and alleged that these claims are anticipated by Lakowicz et al. (U.S. Patent No. 6,197,534). Specifically, the Examiner stated that "Lakowicz et al. teach a method for quantifying an analyte in a sample ...." Office Action, page 5. Furthermore, the Examiner posited that "Lakowicz et al. necessarily teach a fusion protein having a dissociation constant of at least 1 mM towards said analyte, and would be so recognized by persons of ordinary skill in the art." Office Action, page 6. Applicants incorporate by reference their comments and arguments previously presented in their Response

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to Office Action of May 9, 2005 and in their Response to Final Office Action of September 2, 2005. Without agreeing with the Examiner's assertion that Lakowicz et al. anticipates the claimed invention, Applicants have amended claim 1 to better capture envisioned commercial embodiments.

As discussed in the interview, it is Applicants' position that Lakowicz does not teach or suggest a fusion protein having a dissociation constant of at least 1 mM, as required by the claims. Rather, Lakowicz teaches a binding protein with a *stronger* affinity than the presently claimed binding protein (*See* Lakowicz et al., col. 12, ll 18-21). Indeed, the limitation "dissociation constant of at least 1 mM" is intended to convey to one of skill in the art that the claimed mutant binding protein possesses a weaker affinity towards its analyte than do proteins disclosed in Lakowicz *et al.* Reconsideration and withdrawal of the Examiner's rejection under 35U.S.C. §102(b) is carnestly solicited.

# C. THE REJECTION OF CLAIMS 14-16 UNDER 35 U.S.C. §103(A) IS NOW MOOT

In the Office Action dated July 29, 2005, the Examiner rejected claims 14-16 and alleged that these claims are obvious in view of Lakowicz *et al.* (U.S. Patent No. 6,197,534) and Tsien & Campbell (U.S. Pregrant Publication No. 2003/0059835). Specifically, the Examiner stated that "it would have been obvious to one of skill in the art to modify the method of Lakowicz *et al.* with the use of DsRed2(C119A) because Tsien & Campbell discovered the importance of C119 in fluorescent protein oligomerization." *Office Action*, page 7. Applicants incorporate by reference their comments and arguments previously presented in their Response to Office Action of May 9, 2005 and in their Response to Final Office Action of September 2, 2005. Without agreeing with the Examiner's assertion that the combination of Lakowicz *et al.* and Tsien & Campbell render claims 14-16 obvious, claim 1 has been amended to better capture commercial embodiments.

As highlighted above and as discussed in the interview, it is Applicants' position that Lakowicz *et al.* does not teach or suggest a functional mutant binding protein with a dissociation constant of at least 1 mM, *i.e.*, a binding protein with *weakened* affinity towards its analyte.

Applicants assert Tsien & Campbell do not rectify these deficiencies. Also discussed in the interview, Applicants assert that the combination of Lakowicz and Tsien & Campbell does not teach each and every limitation of the presently claimed invention. Accordingly, the combination of Lakowicz and Tsien & Campbell can not render the claimed invention obvious under 35 U.S.C. §103. Reconsideration and withdrawal of this rejection are earnestly solicited.

## D. THE DOUBLE PATENTING REJECTIONS

Applicants note that the Examiner's rejections of claims 1-18 under the judicially created doctrine of obviousness-type double patenting are provisional. Therefore, Applicants will address the Examiner's arguments, upon indication of otherwise allowable subject matter.

### III. CONCLUSION

Claims 1, 6 and 12 have been amended and claims 10 and 11 have been canceled. In addition, Applicants assert that the claims, as currently amended do not require a new search over the Examiner's previous search. Furthermore, the claims are novel and non-obvious over the cited references because the references of record do not teach a mutant periplasmic glucosegalactose binding protein with a *weaker* affinity towards its target analyte than that of the wild-type protein. Entry of the claim amendments and reconsideration and withdrawal of all outstanding rejections are earnestly solicited. And allowance of the presently presented claims is earnestly solicited.

Should the Examiner believe that further discussion of any remaining issues would advance the prosecution, he or she is invited to contact the undersigned at the telephone number listed below.

Respectfully submitted, December 21, 2005 A SA Castellano Malm Ferrario & Buck PLLC Вγ Customer Number: 46851 Telephone: (202) 478-5300 Todd B. Buck Facsimile: (202) 318-1288 Registration No. 48,574 CERTIFICATE UNDER 37 CFR 1.8: The undersigned hereby certifies that this correspondence is being facsimile transmitted or being deposited with the United States Postal Service with sufficient postage as first class mail, in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on this 21st day of December 2005 Toll Ada Todd B. Buck Name Signature